MDRD equation estimates of glomerular filtration rate in potential living kidney donors and renal transplant recipients with impaired graft function

Sir,

Reference methods of measuring glomerular filtration rate (GFR) are too time-consuming and expensive for routine clinical use. An alternative approach is to produce estimates of GFR using formulae that are based on biochemical, demographic and anthropometric data. The Levey formula [1] was derived and subsequently validated using data from patients participating in the Modification of Diet in Renal Disease (MDRD) study. It provides a reliable estimate of GFR (MDRD-GFR) for patients with impaired renal function (GFR range (mean ± SD) of 40 ± 20 ml/min/1.73 m² in the MDRD study population). However, Levey emphasized the need for caution in applying the formula to patient subgroups that were not represented in the original study, including renal transplant recipients and individuals with a serum creatinine in the ‘normal’ range [1].

MDRD-GFR (ml/min/1.73 m²)

\[ \text{MDRD-GFR} = 170 \times \left( \text{PCr}^{-0.99} \times \text{age}^{-0.178} \times 0.762 \text{ if patient is female} \right) \times \left( 1.180 \text{ if patient is black} \right) \times \left( \text{SUN}^{0.170} \times \text{Alb}^{-0.318} \right) \]

Where PCr = serum creatinine concentration (mg/dl) (alkaline picrate method); SUN = serum urea nitrogen concentration (mg/dl) (urease method); Alb = serum albumin concentration (g/dl) (bromocresol green method).

Methods. ⁹⁹mTc DTPA-GFR was measured in 33 renal-transplant recipients with chronic allograft nephropathy (group A, 10 female, age range 20–67 years, body mass index 18–32 kg/m²) and 34 potential living kidney donors with ‘normal’ renal function (group B, 18 female, age range 29–66 years, body mass index 19–32 kg/m²). Results were adjusted for body surface area (using the DuBois equation) and for initial disequilibrium of the isotope within its volume of distribution [2,3]. MDRD-GFR was calculated for each individual using data collected at the time of the isotope study, and compared with the corresponding ⁹⁹mTc DTPA-GFR measurement. In group A, additional GFR estimates were obtained using the Nankivell ‘B’ [4] and Walser [5] formulae (derived from renal transplant recipients and ‘low clearance’ chronic renal failure patients, respectively). Bias plots were constructed using Microsoft Excel ‘Analyse-it’ software [6].

Results. The median values of the corrected ⁹⁹mTc DTPA-GFR measurements in A and B were 28 (range 15–53) ml/min/1.73 m² and 96 (range 65–126) ml/min/1.73 m². In A, the Levey formula gave the lowest bias (mean difference between ⁹⁹mTc DTPA-GFR and MDRD-GFR) and scatter (median absolute difference between ⁹⁹mTc DTPA-GFR and MDRD-GFR) of the three prediction equations (Figure 1 and Table 1). One patient (AG) was clearly an outlier, with an MDRD-GFR of only 17 ml/min/1.73 m², compared to 35 ml/min/1.73 m² measured by ⁹⁹mTc DTPA. The mean of his measured urea and creatinine clearances (from a 24-h urine collection) was 34 ml/min/1.73 m², suggesting that the MDRD-GFR estimate was inaccurate. The patient was a body-builder with an unusually large muscle mass.

Cockcroft and Gault (C&G) estimates showed a large positive bias, although direct comparison of values is spurious. The C&G formula calculates creatinine clearance rather than GFR. Secondly, the units of C&G estimates are ml/min rather than ml/min/1.73 m², and the most appropriate method of correcting for body surface area is unclear as a weight term is already included in the basic formula.

In group B, MDRD-GFR estimates tended to be lower than ⁹⁹mTc DTPA-GFR (Figure 1), with a bias of 16.6 ml/min/1.73 m² (15.7% of the ⁹⁹mTc DTPA-GFR measurement, 95% confidence interval 11.8–20.8 ml/min/1.73 m²) and a scatter of 17.9 ml/min/1.73 m² compared to 35 ml/min/1.73 m² measured by ⁹⁹mTc DTPA. A difference between GFR values of more than 15 ml/min/1.73 m² was seen only in patients with a ⁹⁹mTc DTPA-GFR measurement that was above 90 ml/min/1.73 m².

Table 1. Bias and scatter values for various prediction equations (group A)

<table>
<thead>
<tr>
<th>Formula</th>
<th>Waaler</th>
<th>Nankivell</th>
<th>Levey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required data</td>
<td>A,G,Cr,Wt,Ht</td>
<td>G,Cr,U,Wt,Ht</td>
<td>A,G,R,Cr,U,Alb</td>
</tr>
<tr>
<td>Bias (95% CI) (ml/min/1.73 m²)</td>
<td>-2 (-4.9 to -0.1)</td>
<td>+7 (+3.6 to +12)</td>
<td>-1 (-3.1 to +1.4)</td>
</tr>
<tr>
<td>Scatter (ml/min/1.73 m²)</td>
<td>4</td>
<td>10</td>
<td>3</td>
</tr>
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</table>

A = age; G = gender; R = race; Cr = serum creatinine; U = serum urea; Alb = serum albumin; Wt = weight; Ht = height.
Discussion. The Levey formula has the advantages of relative simplicity, ease of reporting (anthropometric data are not required), and low cost. Our study suggests that its use in renal transplant recipients with chronic allograft dysfunction is valid unless there is an unusual body composition. However, it tends to underestimate GFR in patients with normal or mildly impaired renal function as measured by a reference isotopic method ($^{99m}$Tc DTPA-GFR). Similar findings have recently been reported by Bertolatus and Goddard [7]. Refinements of the Levey formula to improve its reliability in the higher GFR range may be determined by further studies involving larger numbers of patients.

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